to deplete to the concentration that will satisfy the operational definition of no residue.

Regulatory method means the aggregate of all experimental procedures for measuring and confirming the presence of the marker residue of the sponsored compound in the target tissue of the target animal.

R_m means the concentration of the marker residue in the target tissue when the residue of carcinogenic concern is equal to S_m in the last tissue to deplete to its permitted concentration.

Residue means any compound present in edible tissues of the target animal which results from the use of the sponsored compound, including the sponsored compound, its metabolites, and any other substances formed in or on food because of the sponsored compound's use.

Residue of carcinogenic concern means all compounds in the total residue of a demonstrated carcinogen excluding any compounds judged by FDA not to present a carcinogenic risk.

S_m means the permitted concentration of residue of carcinogenic concern for a specific edible tissue.

S_o means the concentration of the test compound in the total diet of test animals that corresponds to a maximum lifetime risk of cancer in the test animals of 1 in 1 million. For the purpose of this subpart, FDA will also assume that this S_o will correspond to the concentration of residue of carcinogenic concern in the total human diet that represents no significant increase in the risk of cancer to people.

Sponsor means the person or organization proposing or holding an approval by FDA for the use of a sponsored compound.

Sponsored compound means any drug or food additive or color additive proposed for use, or used, in food-producing animals or in their feed.

Target animals means the production class of animals in which a sponsored compound is proposed or intended for use.

Target tissue means the edible tissue selected to monitor for residues in the target animals, including, where appropriate, milk or eggs.

Test animals means the species selected for use in the toxicity tests.

Threshold assessment means FDA's review of data and information about a sponsored compound to determine whether chronic bioassays in test animals are necessary to resolve questions concerning the carcinogenicity of the compound.

§ 500.84 Operational definition of "no residue".

(a) On the basis of the results of the chronic bioassays and other information, FDA will determine whether any of the substances tested are carcinogenic.

(b) If FDA concludes that the results of the bioassays do not establish carcinogenicity, then FDA will not subject the sponsored compound to the remainder of the requirements of this subpart.

(c) For each sponsored compound that FDA decides should be regulated as a carcinogen, FDA will analyze the data from the bioassays using a statistical extrapolation procedure.

(1) For each substance tested in separate bioassays, FDA will calculate the concentration of the residue of carcinogenic concern that corresponds to a maximum lifetime risk to the test animal of 1 in 1 million. FDA will designate the lowest value obtained as S_o.

(2) FDA will consider that ''no residue'' of the compound remains in the edible tissue when conditions of use of the sponsored compound, including any required preslaughter withdrawal period or milk discard time, ensure that the concentration of the residue of carcinogenic concern in the total diet of people will not exceed S_o. Because the total diet is not derived from food-producing animals, FDA will make corrections for food intake. FDA will designate as S_m the concentration of residue of carcinogenic concern that is permitted in a specific edible product.

§ 500.86 Marker residue and target tissue.

(a) For each edible tissue, the sponsor shall measure the depletion of the residue of carcinogenic concern until its concentration is at or below S_m.

(b) In one or more edible tissues, the sponsor shall also measure the depletion of one or more potential marker residues until the concentration of the

residue of carcinogenic concern is at or below S_m.

(c) From these data, FDA will select a target tissue and a marker residue and designate the concentration of marker residue (R_m) that the regulatory method must be capable of measuring in the target tissue. FDA will select R_m such that the absence of the marker residue in the target tissue above R_m can be taken as confirmation that the residue of carcinogenic concern does not exceed S_m in each of the edible tissues and, therefore, that the residue of carcinogenic concern in the diet of people does not exceed S_o.

(d) When a compound is to be used in milk- or egg-producing animals, milk or eggs must be the target tissue in addition to the tissue selected to monitor for residues in the edible carcass.

(Approved by the Office of Management and Budget under control number 0910–0228)

§ 500.88 Regulatory method.

(a) The sponsor shall submit for evaluation and validation a regulatory method developed to monitor compliance with FDA's operational definition of no residue.

(b) The regulatory method must reliably measure and confirm the identity of the marker residue in the target tissue at concentrations equal to and above R_m.

(c) FDA will publish in the FEDERAL REGISTER the complete regulatory method for measuring the marker residue in the target tissue in accordance with the provisions of sections 409(c)(3)(A), 512(d)(1)(H) and (i), and 721(b)(5)(B) of the act.

(Approved by the Office of Management and Budget under control number 0910–0228)

§ 500.90 Waiver of requirements.

In response to a petition or on the Commissioner's own initiative, the Commissioner may waive, in whole or in part, the requirements of this subpart except those provided under § 500.88. A petition for this waiver may be filed by any person who would be adversely affected by the application of the requirements to a particular compound. The petition shall explain and document why the requirements from which a waiver is requested are not reasonably applicable to the compound, and set forth clearly the reasons why the alternative procedures will provide the basis for concluding that approval of the compound satisfies the requirements of the anticancer provisions of the act. If the Commissioner determines that waiver of any of the requirements of this subpart is appropriate, the Commissioner will state the basis for that determination in the regulation approving marketing of the sponsored compound.

(Approved by the Office of Management and Budget under control number 0910–0228)

§ 500.92 Implementation.

(a) This subpart E applies to all new animal drug applications, food additive petitions, and color additive petitions concerning any compound intended for use in food-producing animals (including supplemental applications and amendments to petitions).

(b) This subpart E also applies in the following manner to compounds already approved:

(1) For those compounds that FDA determines may induce cancer when ingested by man or animals, i.e., suspect carcinogens, §§ 500.80(b), 500.82, and 500.90 apply.

(2) For those compounds that FDA determines have been shown to induce cancer when ingested by man or animals, §§ 500.82 through 500.90 apply.

PART 501—ANIMAL FOOD LABELING

Subpart A—General Provisions

Sec.